

## Evaluation of the success of conservative treatment in spondylodiscitis patients with relevant laboratory findings

Examination of laboratory parameters in spondylodiscitis treatment

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### Abstract

**Aim:** In this study, we aimed to investigate the success of conservative treatment in patients with relevant laboratory findings and early-stage spondylodiscitis. **Material and Methods:** A total of 79 patients (conservative group 38 patients and 41 patients in the surgery group) with early stage spondylodiscitis were included in this study. These patients were divided into two groups as follows: the conservative treatment group included patients in whom conservative treatment was successful, and the surgical treatment group, consisting of patients who underwent surgery due to refractory pain and poor laboratory findings that did not improve despite conservative treatment. Patients underwent laboratory tests twice: first at their initial presentation (initial); then, after antibiotic treatment (end-of-treatment). Laboratory parameters used were C-reactive protein (CRP), white blood count (WBC), platelet count (PLT), erythrocyte sedimentation rate (ESR), neutrophil count, lymphocyte count, monocyte count, NLR, PLR, and MLR ratios.

**Results:** No significant differences were noted between groups in terms of gender, age, and stage. The initial CRP, WBC, neutrophil count, monocyte and platelet were significantly higher in conservative group than in the surgical group. However, there were no significant differences between the groups in the initial ESR, lymphocyte count, NLR, PLR and MLR. The end-of-treatment ESR, WBC, platelet, monocyte, PLR and MLR were significantly higher in the surgical group than in the conservative group. However, there was no significant difference between the groups in the end-of-treatment CRP, neutrophil count, lymphocyte count, NLR.

**Discussion:** Surgery may be considered in patients with spondylodiscitis, when ESR, WBC, platelet, monocyte, PLR, and MLR do not improve with conservative treatment.

### Keywords

Inflammatory Parameters, Spondylodiscitis, Conservative Method, Debridement

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## Introduction

Spondylodiscitis is an infectious disease of the vertebral column that involves intervertebral discs and paraspinal muscles. Initially, it involves the intervertebral disc and vertebral corpus; then, it extends to adjacent vertebrae [1]. The reported incidence of spondylodiscitis is 1/100000, with a mortality rate of 2%–20% [2]. Recently, there has been an increase in the incidence rate due to the emergence of advanced diagnostic tests, increased use of intravenous drugs, and increased bacteremia in immunosuppressed patients [3, 4]. Spondylodiscitis is etiologically classified as granulomatous, pyogenic, and parasitic–fungal [5].

Clinical symptoms, such as pain, fever, and postural disorders, in the vertebral column are used to diagnose spondylodiscitis [6]. The diagnosis should be supported by laboratory findings in addition to clinical findings. Elevated erythrocyte sedimentation rate (ESR), white blood cell count (WBC), and elevated C-reactive protein (CRP) help in the diagnosis of spondylodiscitis [7, 8]. Computed Tomography (CT) is useful for revealing bone defects. Magnetic resonance imaging (MRI) is the imaging technique, which is most commonly used because it can distinguish between infection, malignancies, and degenerative changes, has high sensitivity and specificity and helps with surgical planning [4].

Despite developments in recent years, the diagnosis and treatment of spondylodiscitis remain challenging [9]. The basic principles in the treatment of spondylodiscitis are the elimination of underlying infection using appropriate agents, restoration and preservation of spinal stability, correction of the neurological deficit in the patient, and relief of pain [10]. Conservative treatment can be used in cases when clinical symptoms are mild, bone loss is minimal, and the general condition of the patient poses a high risk for surgery. Indications for surgical treatment include pain that is not relieved by conservative treatment, development of neurological deficits, expected deformity in the spine, development of sepsis, and increased bone loss. In the literature, there are studies that have reported successful results with minimally invasive and open surgery; however, these studies have not categorized patients according to the severity of the disease [11–13]. Akgül et al. classified surgical treatment according to the severity of the disease in patients with spondylodiscitis [14].

Studies in the literature investigating the laboratory findings of spondylodiscitis have focused on CRP, ESR, and WBC [15]. Our study differs from the previous studies that are reported in the literature because we examined the laboratory findings in greater detail and investigated neutrophil, lymphocyte, monocyte counts as well as neutrophil/lymphocyte (NLR), platelet/lymphocyte (PLR), monocyte/lymphocyte (MLR) ratios in addition to the commonly used parameters. This study evaluated the success of conservative treatment in patients with relevant laboratory findings and stage 1–2 spondylodiscitis, classified according to the previous study [14].

## Material and Methods

The archives of Istanbul University, Istanbul Faculty of Medicine, Department of Orthopedics and Traumatology and Department of Infectious Diseases and Clinical Microbiology were screened.

A total of 152 patients treated for spondylodiscitis between 2009 and 2020 were included in the study. Demographic data and radiological images of the patients were extracted from the medical registration system. This study was performed after obtaining the institutional review board approval (2020/9) from our Ethics committee.

The classification system developed by Akgül et al. [14] for spondylodiscitis was followed in our study. This classification classifies all the patients into four stages according to the standard anterior–posterior (AP) and lateral X-ray as well as CT and MRI images. According to Akgül's classification, stage-3 and stage-4 patients met the instability criteria for the spread of the infection. Patients in these stages were not included in our study as they were recommended surgical treatment. For patients in stages 1 and 2, which are classified as early stages, conservative treatment is initially recommended. These patients were divided into two groups as follows: the conservative treatment group, in which conservative treatment was successful, and the surgical treatment group, consisting of patients who underwent surgery due to refractory pain and poor laboratory findings that did not improve despite conservative treatment.

**Inclusion criteria:** The study included patients with stage 1–2 spondylodiscitis and at least one year of follow-up, whose demographic and radiological data were available in the medical registration system.

**Exclusion criteria:** Patients with specific infections, such as tuberculosis and brucellosis, patients who had neurological deficits and epidural abscesses at the time of presentation, and patients classified as stages 3 and 4 (unstable patients) were excluded from the study.

### Management and Following

According to clinical findings and radiological images, patients with a preliminary diagnosis of spondylodiscitis were advised to undergo CT-guided biopsy. Decisions on antimicrobial therapy were given by infectious diseases and clinical microbiology specialists either according to the culture results or empirically. All patients were given a standard 6-week antibiotic therapy, and they were advised to take bed rest. During this period, patients were followed up in the hospital with static thoracolumbar orthosis. If patients acute phase reactants did not improve in patients who achieved relief, and neurological symptoms occurred despite conservative treatment, conservative treatment was considered unsuccessful and surgical treatment was applied.

Patients underwent laboratory tests twice: first at their initial presentation (initial); then, after antibiotic treatment (end-of-treatment). Laboratory parameters used were CRP, WBC, platelet count (PLT), ESR, neutrophil count, lymphocyte count, monocyte count, NLR, PLR, and MLR ratios.

### Statistical Analyses

SPSS software (Version 27.0; SPSS Inc, Chicago, IL, USA) was used for statistical analyses. The normality of distribution was tested using the Shapiro-Wilk test. Descriptive statistical methods were used to evaluate study data including mean, standard deviation, minimum and maximum. Student's t-test was used to compare quantitative data, and Pearson's chi-square test, Fisher-Freeman-Halton test, and Fisher's exact test

were used to compare qualitative variables. A p-value less than 0.05 was considered statistically significant.

Results

A total of 133 patients who met the study criteria were included in the study. Of these, 79 patients were classified as stages 1 and 2. A total of 79 patients (conservative group 38 patients and 41 patients in the surgery group) were included in this study. No significant differences were noted between groups in terms of gender (conservative group: 19 females and 19 males vs. surgery group: 26 females and 15 males;  $p= 0.833$ ), age (conservative group,  $63 \pm 9$  years vs. surgery group,  $63.8 \pm 10$  years;  $p= 0.229$ ), and stage (conservative group, 26 patients with stage 1 and 12 with stage 2 vs. surgery group, 23 patients with stage 1 and 18 with stage 2). The mean follow-up was  $58.6 \pm 30$  (range, 24–140) months in the operated group. The baseline demographic data of these patients are presented in Table 1.

The initial CRP, WBC, neutrophil count, monocyte and platelet were significantly higher in the conservative group than in the surgical group. However, there was no significant difference between the groups in the initial ESR, lymphocyte count, NLR, PLR and MLR.

The end-of-treatment ESR, WBC, platelet, monocyte, PLR and MLR were significantly higher in the surgical group than

in the conservative group. However, there was no significant difference between the groups in the end- of treatment CRP, neutrophil count, lymphocyte count, NLR (Table 2).

Discussion

According to the results of our study, initial CRP, WBC, neutrophil, monocyte, and platelet values were significantly higher in the group with successful conservative treatment than in the surgical treatment group. After medical treatment, ESR, WBC, platelet, monocyte, PLR, and MLR values were found to be significantly higher in the surgical treatment group than in the conservative treatment group. ESR, WBC, platelet, monocytes, PLR, and MLR values, which do not improve with conservative treatment, may be an indicator of surgical treatment in patients with spondylodiscitis.

Spondylodiscitis treatment aims to eliminate infection, stabilize the vertebral column, restore vertebral column function, and relieve pain. The multidisciplinary treatment is managed by infectious diseases and clinical microbiology specialists and spine surgeons. Long-term antibiotic therapy against the disease agent is performed with immobilization as a conservative treatment. Conservative treatment is considered unsuccessful and surgical treatment is applied in the presence of refractory pain, neurological deficits, instability, and deformity of the spine. In our study, antimicrobial therapy was administered to all patients in accordance with the culture results in a biopsy specimen obtained by a CT-guided procedure at the time of admission. Empirical antimicrobial therapy was initiated in patients with no growth in culture to cover both methicillin-resistant staphylococci and gram-negative bacilli, as recommended in the most recent guidelines. Antibiotics were administered to patients for 6 weeks, according to the literature [9, 16]. Patients whose condition failed to improve after 6 weeks of conservative treatment underwent surgery.

Table 1. Demographic data of patients.

	Conservative Group (n:38)		Surgery Group (n:41)		p value
	Mean $\pm$ SD	Min – Max	Mean $\pm$ SD	Min – Max	
Age, years	63 $\pm$ 9	32 – 78	63.8 $\pm$ 10	28 – 82	0,833
Gender, F/M	19/19		26/15		0,229
Stage, 1/2	26.12		23/18		0.259

Table 2. Comparison of laboratory findings of both groups

	Conservative Group		Surgery Group		p value
	Mean $\pm$ SD	Min – Max	Mean $\pm$ SD	Min – Max	
Initial C-reactive protein	141,6 $\pm$ 98	1 – 341	89,9 $\pm$ 82	2 – 452	0.036*
End- of- treatment C-reactive protein	20,5 $\pm$ 12	1 – 45	24,1 $\pm$ 27	1 – 171	0.415
Initial ESR	52,6 $\pm$ 33	2 – 125	67,4 $\pm$ 53	11 – 258	0.150
End of treatment ESR	16,1 $\pm$ 9	5 – 54	54,4 $\pm$ 30	10 – 144	<0.001*
Initial WBC	10200 $\pm$ 3200	1100 – 19600	8300 $\pm$ 2400	4600 – 15500	0.006*
End of treatment WBC	7040 $\pm$ 1400	4500 – 10900	8080 $\pm$ 2700	1300 – 14900	0.040*
Initial Neutrophil	7200 $\pm$ 2450	2500 – 17900	5270 $\pm$ 2700	1000-10200	<0.001*
End- of- treatment Neutrophil	4390 $\pm$ 850	2800 – 6000	3570 $\pm$ 2600	600 – 11100	0.105
Initial Lymphocyte	1450 $\pm$ 500	900 – 3300	1509 $\pm$ 1380	500 – 6900	0.876
End- of- treatment Lymphocyte	820 $\pm$ 330	400 – 2000	1050 $\pm$ 1200	200 – 5600	0.289
Initial Platelet	379000 $\pm$ 64000	294000 – 619000	295000 $\pm$ 87000	27000 – 500000	<0.001*
End- of- treatment Platelet	265000 $\pm$ 47000	163000 – 460000	555000 $\pm$ 300000	215000 – 1300000	<0.001*
Initial monocyte	875 $\pm$ 128	450 – 1000	713 $\pm$ 341	200 – 2000	0.008*
End- of- treatment monocyte	500 $\pm$ 116	300 – 800	915 $\pm$ 767	300 – 5400	0.002*
Initial NLR	5.07 $\pm$ 1.4	1.9 – 8.4	5.32 $\pm$ 3.7	0.3 – 14.7	0.698
End- of- treatment NLR	5.88 $\pm$ 1.8	2.7 – 11.5	5.45 $\pm$ 5.2	0.5 – 20.4	0.648
Initial PLR	282 $\pm$ 87	89 – 422	294 $\pm$ 182	34 – 750	0.722
End- of- treatment PLR	363 $\pm$ 133	128 – 675	1456 $\pm$ 1302	57 – 4153	<0.001*
Initial MLR	0.653 $\pm$ 0.2	0.20 – 1	0.746 $\pm$ 0.53	0.10 – 2.20	0.327
End- of- treatment MLR	0.689 $\pm$ 0.2	0.20 – 1.3	2.51 $\pm$ 4.4	0.12 – 28.8	0.013*

Laboratory findings were recorded for patients in both groups before and after treatment.

In terms of surgical treatment selection, existing classification systems in the literature are insufficient. Akbar et al. developed the physical status classification system, which provides information on the general treatment procedure based on instability and neurological condition [17]. Similar criteria have been used in the classification system developed by Pola et al. [12]. According to the severity of the disease, Akgül et al. developed a classification system that determines the choice of surgical treatment. Hence, the patients in our study were classified using this classification system. This study aimed to show the relationship between the failure of conservative treatment and laboratory findings for patients classified as stages 1 and 2 according to the same staging approach.

To date, no consensus has been reached on the surgical treatment of early-stage spondylodiscitis. Many studies have indicated that patients who receive long-term antibiotic treatment without surgical debridement may develop deformity and instability in the affected areas of the spine [16]. In a classification of Akgül et al., stages 1 and 2 are classified as early stages; surgical treatment is recommended in the presence of non-specific refractory pain and persistently poor laboratory findings despite antibiotic therapy in these stages. In our study, 79 of the 133 patients were classified as stages 1 and 2. Of these, 38 patients achieved successful results with conservative treatment; 54 patients with poor laboratory findings and concomitant chronic pain required surgical treatment at the end of 6 weeks.

Spondylodiscitis does not present specific symptoms; therefore, its diagnosis may be delayed by 2–6 months [9]. Patients who cannot be diagnosed early may present with advanced bone loss and deformity in the vertebral column; according to Akgül et al., stage 3–4 patients fall into this group. In these patients, the most common reason for surgery is deformity and instability rather than infection. In our study, 48 patients were classified as stages 3–4. All of these patients underwent surgical treatment due to concomitant chronic pain, deformity, and instability. Clinical and laboratory results of the patients improved with surgical treatment.

Studies in the literature investigating the laboratory findings of spondylodiscitis have focused on CRP, ESR, and WBC [15]. Laboratory findings and radiological imaging can be used in the diagnosis of vertebral infections as well as in the monitoring of treatment [17]. ESR is often reported to be elevated in spinal infections [18]. The mean ESR in vertebral infections was 84.5 mm/hour in one study and 70.4 mm/hour in another study [19]. There are studies indicating that CRP is beneficial in the early diagnosis of postoperative discitis [20]. According to these studies, CRP returns to normal levels faster than ESR after treatment. A study has also examined CRP and WBC levels of patients with spondylodiscitis who received conservative and surgical treatment [15]. Another study examined CRP and WBC levels in patients with spondylodiscitis who were conservatively or surgically treated. The same study reported that WBC count did not show interpretable profiles between the two groups [20]. In our study, although CRP, WBC, neutrophil count, monocyte, and platelet values were significantly higher initially in the

group with successful conservative treatment than the surgical treatment group, these levels improved faster in the same group with medical treatment than in the surgical treatment group.

Our study differs from the previous studies that are reported in the literature because we examined the laboratory findings in greater detail and investigated neutrophil, lymphocyte, monocyte counts as well as NLR, PLR, MLR levels in addition to the commonly used parameters. Monocytes originate in progenitor cells in the bone marrow; circulating monocytes migrate to tissues where they differentiate during hemostasis and infection, thereby contributing to the body's defense mechanism [21]. Blood platelets are involved in both acute and chronic inflammation [22]. Recent studies have revealed that NLR, PLR, and MLR are new inflammatory markers that can be used to diagnose and predict the prognosis of a variety of infectious diseases. Furthermore, their levels increase during infections [23–25]. PLR and MLR levels in this study were not observed to be statistically different between the two groups at the start of treatment; however, after medical treatment, they significantly increased in the surgical treatment group compared to the group that had successful conservative treatment. Poor outcomes at these levels that do not improve despite treatment can indicate the failure of conservative treatment.

Our study has some limitations. The staging system that we used does not include patient-specific factors and comorbidities. Another limitation is the retrospective design of our study.

### Conclusion

Stages 1 and 2 are categorized as early stages in the classification system of Akgül et al. Patients who do not benefit from conservative treatment can undergo surgical treatment. Surgery may be considered in patients with spondylodiscitis, when ESR, WBC, platelet, monocyte, PLR, and MLR do not improve with conservative treatment.

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### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

### Animal and human rights statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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### Conflict of interest

The author(s) declared no conflicts of interest.

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